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Published:

with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MORPHOLINE DERIVATIVES WITH A SUBSTITUTED ACETAMIDE GROUP IN THE 2-POSITION FOR USE AS CCR-3 ANTAGONISTS FOR THE TREATMENT OF INFLAMMATORY DISEASES

$$R^{1}$$
 X
 N
 R^{3}
 R^{10}
 R^{2}

(57) Abstract: Certain compounds of formula (I); wherein R_1 represents substituted or unsubstituted aryl; X represents -O-or a bond; Y represents -(CR_{na},R_{nb}) n-; R_{na} and R_{nb} are each independently hydrogen or C₁₋₆alkyl; n is an integer from 1 to 5; R^2 represents unsubstituted or substituted aryl or unsubstituted or substituted heteroaryl; R^3 represents hydrogen or C₁₋₆alkyl; R^{10} represents hydrogen or C₁₋₆alkyl; and salts and solvates thereof are CCR3 antagonists and are therefore indicated to be useful in therapy of inflammatory conditions.



Internation Application No. PCT/EP 03/03348

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/5377 A61K31/5375 CO7D413/12

C. DOCUMENTS CONSIDERED TO BE RELEVANT

A61P29/00 C07D413/06 CO7D209/48 A61P11/06

CO7D265/30

Relevant to claim No.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Category °

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BEILSTEIN Data, CHEM ABS Data

Citation of document, with indication, where appropriate, of the relevant passages

	1–24						
SELECTIVE AND POTENT GASTRIC F AGENTS 1. SYNTHESIS AND STRUCT RELATIONSHIPS OF N-(2-MORPHOLINYL)ALKYLBENZAMIC JOURNAL OF MEDICINAL CHEMISTRY CHEMICAL SOCIETY. WASHINGTON,	19						
χ Further documents are listed in the continuation of box C. χ Patent family members are listed in annex.							
ategories of cited documents: ment defining the general state of the art which is not idered to be of particular relevance document but published on or after the international date tent which may throw doubts on priority claim(s) or n is cited to establish the publication date of another on or other special reason (as specified) ment referring to an oral disclosure, use, exhibition or means tent published prior to the international filling date but than the priority date claimed	cited to understand the principle or the invention "X" document of particular relevance; the cannot be considered novel or cannot involve an inventive step when the document of particular relevance; the cannot be considered to involve an indocument is combined with one or ments, such combination being obvion in the art.	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled					
actual completion of the international search	Date of malling of the international se	arch report					
7 July 2003	18/07/2003						
mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Johnson, C						
	DUNCAN BRUCE (GB); GLAXO GROUP 4 April 2002 (2002-04-04) examples claim 1 KATO SET AL: "NOVEL BENZAMID SELECTIVE AND POTENT GASTRIC P AGENTS 1. SYNTHESIS AND STRUCT RELATIONSHIPS OF N-(2-MORPHOLINYL)ALKYLBENZAMID JOURNAL OF MEDICINAL CHEMISTRY CHEMICAL SOCIETY. WASHINGTON, vol. 33, no. 5, May 1990 (1990) 1406-1413, XP001037844 ISSN: 0022-2623 example 9 ther documents are listed in the continuation of box C. ategories of cited documents: then defining the general state of the art which is not dered to be of particular relevance document but published on or after the international date ent which may throw doubts on priority claim(s) or is cited to establish the publication date of another one or other special reason (as specified) nent referring to an oral disclosure, use, exhibition or means than the priority date claimed rectual completion of the international filling date but than the priority date claimed rectual completion of the international search 7 July 2003 mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo ni,	examples claim 1 KATO S ET AL: "NOVEL BENZAMIDES AS SELECTIVE AND POTENT GASTRIC PROKINETIC AGENTS 1. SYNTHESIS AND STRUCTURE—ACTIVITY RELATIONSHIPS OF N—(2—MORPHOLINYL)ALKYLBENZAMIDES" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 33, no. 5, May 1990 (1990–05), pages 1406–1413, XP001037844 ISSN: 0022–2623 example 9 -/ ther documents are listed in the continuation of box C. Italian to be of particular relevance of document but published on or after the international date of another on or other special reason (as specified) ent which may throw doubts on priority claim(s) or its cited to establish the publication date of another on or other special reason (as specified) ent referring to an oral disclosure, use, exhibition or means then the priority date claimed A claim of the international filling date but than the priority date claimed A claim of the international search Date of mailting of the international search					



Internat Application No PCT/EP 03/03348

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT								
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.						
A	WO 00 31032 A (HOFFMANN LA ROCHE) 2 June 2000 (2000-06-02) page 2, line 25 - line 27; claim 1	1-24						

International Application No. PCTEP 03 03348

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 18,19 (part)

The compounds of claims 18 and 19 contain a substituent A, which is defined as a "protected amino group". However, this definition is only clear when the reaction conditions in which the amine remains protected, and those in which it is deprotected are specified. This is not the case in present claims 18 and 19. The broadest definition which is unambiguously clear has been used in the search, namely A = Phthalimido (p. 28).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.



International Internation No. PCT/EP 03/03348

Box ! Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)						
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:						
1. X Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:						
Although claim 23 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.						
2. X Claims Nos.: 18,19 (part) because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:						
see FURTHER INFORMATION sheet PCT/ISA/210						
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).						
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)						
This International Searching Authority found multiple inventions in this international application, as follows:						
As all required additional search fees were timely paid by the applicant, this international Search Report covers all searchable claims.						
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.						
3. As only some of the required additional search fees were timely paid by the applicant, this international Search Report covers only those claims for which fees were paid, specifically claims Nos.:						
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:						
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.						

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